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MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Worker and Residential/Bystander Risk Assessment Of Metam Sodium During Soil Applications.

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Attached is the risk assessment for occupational and residential exposures to Metam Sodium during soil applications, only. This assessment estimates the short-term risk to workers: mixer/loaders and applicators; and residents who live downwind from field applications. HED team members from OREB, Tox II, and CCB reviewed this document and their comments have been incorporated into the revised risk assessment. If you have any questions please contact Ameesha Mehta at 305-6703.

Attachment

cc: Larry Dorsey
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HED Metam-sodium Team Members: (Members responsible for review of technical accuracy, selection of NOEL's as the basis for MOE estimates, issues presented and policies as relevant to this risk assessment.)

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I. INTRODUCTION

A. Background

Metam sodium (sodium-N-methyldithiocarbamate), also known as Vapam, Metham sodium and SMDC, has the following physical and chemical properties:

CAS No.	CAS 137-42-8
Physical State	Light yellow liquid
Molecular Weight	129
Water Solubility	722 g/L at 20°C
Vapor Pressure	21 mm Hg
pH:	9.0-10.5
Odor:	Strong, sulfur-like

Metam sodium is a fumigant-type pesticide with end-use products formulated as 18 to 42% aqueous solutions. This chemical, registered since 1954, is a pesticide used as a preplant fumigant to control weeds, nematodes, fungi, bacteria and insects. There are approximately 35 different metam sodium products registered for a variety of uses. Some of the different use patterns include agricultural preplant soil fumigation, wood preservative, slimicide, tree-root killer and aquatic weed control. Approximately 10 million pounds of the active ingredient (a.i.) were used in 1990, with 40-45% used for agricultural purposes.

Metam-sodium (Vapam) is a non-selective preplant fumigant for control of weeds, soilborne diseases, and nematodes infesting field and vegetable crops. It is applied at least 14 to 21 days prior to planting by some of the following methods: shank injection, rotary tiller, solid set sprinkler, and center pivot chemigation. The formulated product is a water miscible concentrate containing 3.18 lbs ai/gallon. Metam sodium when mixed with water hydrolyses to Methyl isothiocyanate (MITC), and Carbon disulfide (CS₂).

B. Purpose

In September 1991, the Environmental Protection Agency negotiated a settlement agreement with the Metam Sodium Task Force (MSTF). This settlement agreement was prompted by the July 14, 1991 spill of thousands of gallons of metam sodium into the Sacramento River near Dunsmuir, California. As per the settlement agreement and for reregistration purposes, the MSTF was required to conduct several toxicity and exposure studies. Therefore, Special Review and Reregistration Division (SRRD) has requested that HED review the studies and assess both worker and residential risk. Note that metam sodium is also being tracked by Special Review as an alternative to Telone for soil uses. Therefore, this document will only address metam sodium worker and residential risk as it pertains to the agricultural (soil) uses.

II. HAZARD IDENTIFICATION

A. Toxicology Database

Please see the appendix for a summary of the historical Toxicology database for metam sodium. (T. McMahon/HED, 7/27/93)

B. Acute Toxicity

The acute oral LD₅₀ of 43.7% technical metam sodium in rats is 870 mg/kg in males and 924 mg/kg in females (Tox. Category III); the acute dermal LD₅₀ using technical material (approximately 43% active ingredient) in male and female rabbits is 368 mg/kg (Tox. Category III). The acute inhalation LC₅₀ in rats is 2.275 mg/L (Tox. Category III). Metam sodium is slightly irritating to the eyes (Tox. Category III), and is a moderate to severe dermal irritant (Tox. Category II) and a skin sensitizer.

1. Metam Sodium Neurotoxicity Study in Rats, MRID # 429778-01

A definitive acute neurotoxicity study was conducted in male and female Sprague-Dawley rats using dose levels of 0, 50, 750 or 1500 mg/kg. There were 12 rats/sex/dose except for the highest dose which had 16 rats/sex/dose. Based on percent active ingredient (43.15%), actual doses were 0, 22, 324, or 647 mg/kg. Viability, clinical signs, body weights, functional observational battery, and motor activity were evaluated.

Mortality was observed at the 647 mg/kg dose level, where a total of 5 males and 3 females were found dead during the study. Signs of systemic toxicity were observed at the 324 and 647 mg/kg dose levels, and included alterations in posture and palpebral closure, increased lacrimation and salivation, alterations in respiratory rate, decreased arousal, decreased rearing activity, increased time to first step, lack of approach, olfactory, and pupil responses, absent or reduced tail pinch response, reduced hindlimb strength, and decreased body temperature and body weight. Reductions in mean ambulatory and total motor activity were observed at the 22 mg/kg dose level and above. Inhibition of plasma and red cell cholinesterase was observed at the 647 mg/kg dose level in male and female rats 24 hours post-dose. The LOEL of 22 mg/kg was based on reduced ambulatory and total motor activity observed in the male and female rats. The NOEL was determined to be < 22 mg/kg (lowest dose tested) and was not achieved in this study. (T. McMahon/HED, 3/11/94)

C. Developmental and Reproductive Toxicity

The Health Effects Division Peer Review Committee (PRC) for Developmental and Reproductive Toxicity concluded, December 12, 1991, that metam sodium induces developmental toxicity in 2 species (rat and rabbit) albeit neither study was considered to be fully adequate due to deficiencies in study design and reporting. (G. Burin/HED, 3/27/92)

In October 1993, the MSTF submitted to the Agency a Rat Developmental Toxicity Study under FIFRA Section 6(a)(2) and a Rabbit Developmental Toxicity Study. Toxicology Branch II reviewed the studies in December 1993 and found both studies to meet core guideline requirements, and hence, appropriate NOEL's for developmental toxicity were established.

1. Developmental Study in the Rat, MRID # 429837-01

In a developmental toxicity (teratology) study, rats of the Wistar strain from the Barrired Animal Breeding Unit, Biological Services Section, Zeneca Central Toxicology Laboratory, Cheshire, UK received 0, 5, 20, or 60 mg/kg/day metam sodium by oral gavage on gestation days 6 through 17 inclusive. Insemination was by natural means. Test compound (43% w/w active ingredient in aqueous solution, 525.54 g/L, batch no. BAS/OO5/OON) was adjusted for the above doses.

Maternal toxicity was noted at the 20 and 60 mg/kg/day dose levels in the form of decreased body weight gain during the period of treatment, and a decrease in food efficiency during test article administration. The decrease in food efficiency supports a test article related effect during the period of dosing. Therefore, the Maternal Toxicity NOEL = 5 mg/kg/day, and the Maternal Toxicity LOEL = 20 mg/kg/day based on reduced body weight gain and decreased food efficiency.

Developmental toxicity was suggested at 20 and 60 mg/kg/day on the fetal and litter basis as increased incidences of unossified centrum of the 4th, 5th, and 6th cervical vertebrae. Also at 20 and 60 mg/kg/day unossified odontoid, centrum of the 2nd cervical vertebra, ventral tubercle, and calcaneum were observed on the fetal basis. A significant decrease in mean fetal weight was observed at the 20 and 60 mg/kg/day dose levels. The number of resorptions/dam and the incidence of unossified 5th sternbrae was significantly increased on litter basis at 60 mg/kg/day. In this investigation, the developmental toxicity NOEL was 5 mg/kg/day and the developmental toxicity LOEL was 20 mg/kg/day based on the increased incidence of skeletal observations and the increase in resorptions/dam.

This study was classified as Core Guideline data and satisfied the 1984 Guideline Requirement (§83-3a) for a developmental toxicity (teratology) study in rats. (T. McMahon/HED, 12/7/93)

2. Developmental Toxicity Study in the Rabbit, MRID #429631-01

In a developmental toxicity (teratology) study, New Zealand White rabbits from Interfauna UK Ltd, Huntingdon, Cambridgeshire, UK, received 0, 5, 20 or 60 mg/kg/day metam sodium by oral gavage from gestation days 8 through 20, inclusive. The animals were received time-pregnant from the vendor. The test compound 43.14% w/w active ingredient concentration in liquid form (525.54 g/L, Batch 90/2, Y06930/007/001 and YA6930/008) was adjusted for the above doses.

Maternal toxicity was noted in the mid and high dose groups in the form of increased incidences of decreased feces and red/orange staining on the cage tray in the 60 mg/kg/day metam sodium group compared with the control group. In addition, a treatment related decrease in body weight gain in the mid and high dose groups during the dosing period was observed with a rebound in the high dose group. Decreases in corrected body weight gain were also observed during the dosing, post dosing, and entire gestation periods (excluding days 0-4). Food consumption was reduced in the mid and high dose groups during the dosing period, with a rebound in food consumption to control levels in the high dose group following dosing. Food efficiency was reduced during the dosing period, post dosing period, and entire gestation period (minus gd 0-4). The corrected body weights for the mid and high dose groups were also reduced. This evidence of toxicity supports the body weight gain findings. Therefore, the Maternal Toxicity NOEL = 5 mg/kg/day, and the Maternal Toxicity LOEL = 20 mg/kg/day based on the reduced body weight gain, reduced food consumption and food efficiency.

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Developmental toxicity was noted in the high dose group in the form of increased resorptions including total litter resorptions, a decrease in the number of live fetuses/dam, mean litter size, and an increase in post-implantation loss. There was also a decrease in mean fetal body weight noted in the high dose group. Developmental toxicity was noted in the mid dose group in the form of increased incidences of sutural bones between the parietals, misshapen hyoid, partially ossified transverse process of the cervical vertebrae, and 27 presacral vertebrae. There was an increased incidence in the high dose group in the 27 presacral vertebrae and 7 sternbrae (usually only 6 present). Therefore, the Developmental Toxicity NOEL = 5 mg/kg/day and the Developmental Toxicity LOEL = 20 mg/kg/day based on the increased incidence of skeletal observations.

This study was classified as core minimum data and satisfies the 1984 Guideline Requirement (§83-3 b) for a developmental toxicity (teratology) study in rabbits. (T. McMahon/HED, 12/7/93)

**3. Metam Sodium: 2-Generation Reproduction Study in Rats:
MRID # 431361-01**

In a multigeneration reproduction study, male and female Alpk:APfSD rats (30 /sex/dose), obtained from the Specific Pathogen Free (SPF) colony at the Barriered Animal Breeding Unit at Zeneca Pharmaceuticals, Alderley Park, Macclesfield, Cheshire, UK received the following doses of metam sodium in drinking water: 0, 0.01, 0.03, or 0.1 mg/mL. These levels correspond to 0, 1.2, 3.2, or 11.5 mg/kg/day for males and 0, 1.8, 3.9 or 13.5 mg/kg/day for females. Treated drinking water was administered continuously throughout the study. After the first 10 weeks, animals were mated on a one-to-one ratio. At 21 days of age, pups from the F₀ generation were selected as parents for the F₁ generation (30/sex/group).

Systemic toxicity was observed at the 0.1 mg/mL dose level in adult female rats of the F₀ and F₁ generations. This toxicity consisted of Bowman's gland duct hypertrophy with loss of alveolar cells, degeneration/disorganization and/or atrophy of the olfactory epithelium, and dilation of the Bowman's gland ducts. The change in Bowman's glands were accompanied in all affected animals by degeneration, disorganization, and/or atrophy of the olfactory epithelium. In pups, findings were limited to, and observed mainly at, the high dose. These consisted of a decrease in mean pup weight of 14% vs control on day 22 for the F₁ parents, a 16% decrease in body weight gain for male and female pups in the F₂ litter at the high dose, and decreases of 8-9% in testes and epididymis weights for male pups in the F₁ and F₂ litters at the high dose. The systemic NOEL was 0.03 mg/mL [3.2 mg/kg/day (males) and 3.9 mg/kg/day (females)], and the systemic LOEL was 0.1 mg/mL [11.5 mg/kg/day (males), and 13.5 mg/kg/day (females)]. There were no apparent effects of metam sodium on reproductive performance in the F₀ and F₁ generations in this study. The reproductive NOEL was 0.1 mg/mL and the LOEL for reproductive toxicity was > 0.1 mg/mL. This study has been classified as core minimum data and satisfies the guideline requirement (§83-4) for a multigeneration reproduction study in rats. (T. McMahon/HED, 4/19/93)

D. Subchronic Toxicity Data

1. Metam Sodium: 90-Day Oral Dosing Study in Dogs: MRID# 426000-01

Metam sodium was administered by gelatin capsule to male and female dogs at nominal dose levels of 0, 1, 5, or 10 mg/kg/day once daily for 13 weeks. Toxic effects were observed at all dose levels tested, but were primarily evident at the 5 and 10 mg/kg/day dose groups. They included significant increases in plasma ALT, AST, ALK PHOS, and GGT (including significantly increased ALT in female dogs at 1 mg/kg/day); increased amounts of blood, urobilinogen, bilirubin, and protein in urine; and microscopic evidence of hepatitis. At the 10 mg/kg/day dose group, the following toxic effects were observed: decreased body weight and body weight gain in male and female dogs; and hematologic alterations (increased cell volume, cell hemoglobin, neutrophils, and monocytes; decreased MCHC). A majority of the toxic effects observed in this study appeared dose- and time-related in treated dogs. No evidence of tumors was found in this study.

Based upon the results of this study, the systemic NOEL was < 1 mg/kg/day, and systemic LOEL was \leq 1 mg/kg/day for female dogs, based upon the increase in plasma ALT and biliary duct proliferation with inflammatory cell infiltration. For male dogs, the systemic NOEL was = 1 mg/kg/day and systemic LOEL = 5 mg/kg/day, based upon statistically significant increases in plasma ALT, AST, and alkaline phosphatase, as well as the increased incidence of hepatitis and bile duct proliferation.

This study did not satisfy the guideline requirement (§82-1) for a subchronic toxicity study in dogs, due to the lack of establishment of a systemic NOEL for toxicity. It has been classified as core supplementary. (T. McMahon/HED, 2/12/94)

2. Metam Sodium: 90-Day Drinking Water Study in Rats: MRID# 421173-02

In this study, metam sodium was administered to male and female rats in drinking water at nominal dose levels of 0, 0.018, 0.089 or 0.443 mg/mL (0, 1.7, 8.1, or 26.9 mg/kg/day in males; 0, 2.5, 9.3, or 30.6 mg/kg/day in females). At the high dose in both sexes, systemic toxicity in the form of significantly decreased food and water consumption, decreased body weight gain, and histological changes in the nasal cavity olfactory epithelium were observed. Also at the high dose, renal tubular dilation and basophilia, along with increases in blood, protein, and red cells in urine were also observed. High dose males exhibited an increased incidence of plasma cell hyperplasia in cervical lymph nodes and a significant decrease in platelet count. A significant decrease in group mean body weight was observed in female rats at the mid dose, and body weight gain was decreased 11% at the high dose for the duration of the study. Significant decreases in red cell count and hematocrit were also observed at the mid dose in both sexes.

Tentative NOEL = 1.7 mg/kg/day (males); 2.5 mg/kg/day (females)
Tentative LOEL = 8.1 mg/kg/day (males); hematological changes; 9.3 mg/kg/day (females); decreased absolute body weight.

Tentative MTD = 26.9 mg/kg/day (males); 30.6 mg/kg/day (females); decreased absolute body weight, body weight gain; alterations in hematology and clinical chemistry parameters; increased incidence of histopathological abnormalities.

This study has been classified as supplementary, and it does not satisfy the guideline requirement (§82-1) for a subchronic toxicity study in rats. (T. McMahon/HED, 4/21/94)

3. Metam Sodium: 90-Day Drinking Water Study in Mice with a 28-Day Interim Kill: MRID # 421173-01

Metam sodium was administered to male and female mice in the drinking water at dose levels of 0, 0.018, 0.088, 0.35, or 0.62 mg/mL for 90 days. These doses correspond to 2.7, 11.7, 52.4, or 78.7 mg/kg/day for males; and 3.6, 15.2, 55.4, or 83.8 mg/kg/day for females. The systemic toxicity NOEL was 0.018 mg/mL and the LOEL was 0.088 mg/mL based on urinary bladder lesions (eosinophilic granules, cystitis and mucosal hyperplasia) in both sexes and decreases in hematology parameter values (hemoglobin, red blood cells, hematocrit) in female mice. Based on decreased body weight gains, the MTD appears to have been achieved at 0.35 mg/mL in males and 0.62 mg/mL in females. This study has been classified as supplementary (Y. Ioannou/HED, 5/14/92)

E. Chronic Toxicity Data

On April 20, 1994 the MSTF submitted to the agency a 6(a)(2) notification letter reporting preliminary data for the two year drinking water study in mice. The final study report was submitted to the Agency in May 1994, and is in the review process. Groups of 55 mice/sex/group were administered drinking water containing 0, 0.019, 0.074, or 0.23 mg/mL metam sodium for a period of two years. The administration of metam sodium had no adverse effects on the survival and no clinical signs of toxicity were apparent. However, treatment with the 0.23 mg/mL (HDT) metam sodium was associated with an increased incidence of angiosarcoma in males and females. This two year mice drinking water study is in the HED review process. According to SRRD, the combined chronic/carcinogenicity rat and dog studies were due to the Agency on May 31, 1994.

F. Mutagenicity Studies

Metam sodium was negative for bacterial gene mutation in Salmonella typhimurium strains when tested at levels up to 2500 ug/plate with and without metabolic activation (MRID # 403056-03). Metam sodium gave a positive response in an in vitro cytogenetic assay at 20 ug/mL without metabolic activation or at 20 and 40 ug/mL with metabolic activation using cultured human lymphocytes (MRID # 403056-04). It was, however, negative in an in vitro Chinese hamster bone marrow cytogenetic assay (MRID # 403056-05). Metam sodium was also negative in an unscheduled DNA synthesis assay using primary rat hepatocytes (MRID # 403056-01).

G. Metabolism/Pharmacokinetic Data

Administration of ¹⁴C-metam sodium to male and female rats either as a single oral dose (10 mg/kg) or as a high single oral dose (100 mg/kg) resulted in rapid absorption through the gastrointestinal tract and distribution to all examined tissues. **Metam sodium is primarily metabolized to MITC and carbon disulfide in the body at a ratio of approximately three to one.** Both of these metabolic products undergo further metabolism by different pathways, with the products of MITC excreted in the urine and the products of carbon disulfide eliminated by exhalation. Over 80 percent of the administered radioactivity was excreted within 24 hours in both sexes. Elimination was mainly through the urine and the expired air with lesser amounts in the feces in both sexes at either the low or the high dose. Elimination of radioactivity after 24 hours appeared to be very slow resulting in a half-life ranging from 61 to 74 hours. Peak plasma concentrations of radioactivity were observed within one hour after

administration in male and female rats at both dose levels tested. Tissue concentrations were highest in thyroid gland, liver and kidneys seven days after administration. No parent compound was detected in the urine or the expired air. Metabolites identified in the expired air were MITC, CO₂, and CS₂/COS. In urine, up to five metabolites were isolated but only one of these metabolites was positively identified as N-acetyl-S-(N-methylthiocarbamoyl)-L-cysteine, presumably the conjugation product of MITC and glutathione. (S. Stolzenberg/HED, 9/30/88)

H. *Structure Activity Relationships*

Metam sodium is structurally related to several compounds belonging to the general class of dithiocarbamates (all derivatives of dithiocarbamic acid). Partial developmental and/or reproductive toxicity data exist for some of these chemicals including Dazomet, Maneb, Zineb, Metiran, Nabam, Ziram, Vancide, Busan-85, and Thiram. From the available data, Nabam, Thiram, Vancide, Busan-85 and Dazomet appear to be of concern for developmental toxicity. Carbon disulfide appears to be a common metabolite for these chemicals. However, of the above chemicals, only Dazomet is known to be metabolized to MITC. Metam sodium is readily metabolized mainly to MITC and CS₂.

1. **Methyl isothiocyanate (MITC)**

MITC is highly toxic by the dermal (LD₅₀ 145 mg/kg) and inhalation (LC₅₀ < 0.03 mg/L) routes of exposure (Tox. Category I). It is also a severe eye and dermal irritant (Tox. Category I).

MITC has an odor detection threshold value of 100 to 500 ppb (0.13 to 15 mg/m³) in air and a characteristic "horseradish" smell. In general, detection odor thresholds are relatively unreliable and difficult to reproduce because they are based on a poorly defined judgement of the observer. Consequently, the concentration at which the precise odor of MITC can be identified has not been measured.

MITC has been tested for developmental toxicity in the rat by gavage at 0, 1.0, 5.0, or 25 mg/kg/day, days 6-15 of gestation (Accession # 257765). The maternal NOEL was established at 5 mg/kg/day. The maternal LOEL was 25 mg/kg/day based on decreases in maternal weight gain and food consumption during the dosing period. In addition, the corrected maternal weight gain was also affected (absolute weight gain minus gravid uterine weight). Mean fetal weight and crown rump length were significantly reduced at 25 mg/kg. Individual litter data were not submitted with this report and, therefore, it was not possible to calculate the litter incidence for the malformations or variations that were observed. Fetuses with more than one finding may have been reported more than once. An increased incidence of unilateral lens opacity was noted in the skeletal fetuses in all treated groups compared to the concurrent control. The frequency of fetuses with lens opacity was not reported for fetuses fixed in Bouin's solution. Historical control data for lens opacity was also not reported. Overall there was an apparent increase in the incidence of fetuses with malformations and variations at 25 mg/kg compared to the concurrent control. However calculation of the total number of fetuses with malformations or the percentage of litters affected could not be assessed due to the lack of individual animal data. Therefore, the developmental NOEL could not be determined. Preliminary review of a current submission to upgrade this study does not appear to be adequate.

MITC was administered to New Zealand White rabbits by gavage days 7-19 of gestation at 0, 1, 3, or 5 mg/kg/day (Accession # 257764). The maternal NOEL was > 5 mg/kg/day (HDT). The HED Reproductive and Developmental Toxicity Peer Review Committee during their deliberations for metam sodium indicated that the developmental NOEL in this investigation was tentatively established at 3 mg/kg/day (G. Burin/HED, 3/27/92). The developmental LOEL was 5 mg/kg/day based on growth retardation, and an increased incidence of bilateral lens opacity and fused sternalbrae in the absence of maternal toxicity.

MITC is the principal decomposition product and metabolite of metam sodium. Neurotoxicity screening studies have been recommended for MITC (B. Sette, 7/9/91).

According to a DCI issued July 1991, EPA required the following studies from the MITC registrants and were to be completed by July 1994: §81-4 Primary Eye Irritation §81-6 Dermal Sensitization (rabbit); §83-4 Two-Generation Reproduction (rat); §84-2 Gene Mutation (Ames test); and §85-1 General Metabolism.

The following MITC studies are currently under review in Toxicology Branch II: §81-6 Dermal Sensitization (MRID 41221404), §82-2 21-day Dermal (MRID 41221406), §82-4 90-day Inhalation rat (MRID41221407), §83-3 Developmental Toxicity (MRID 00150076 and 00150077), §84-2 Gene Mutation (MRID 41221410), and §84-4 Other Genotoxic Effects SCE in Chinese Hamster V79 cells (MRID 41221412). The 2 Generation Reproduction and General Metabolism study requirements have been waived since MITC is not considered to be a food use chemical.

2. Carbon disulfide (CS₂)

Hardin et al., in 1981, evaluated CS₂ developmental toxicity in Sprague-Dawley rats and New Zealand white rabbits. The authors indicated that the results they were reporting, for a number of workplace chemicals, were from studies conducted in both the NIOSH Cincinnati facilities as well as laboratories under contract with NIOSH. The concentrations under test were selected from published toxicology data. The recommended occupational exposure limits (i.e. the Occupational Safety and Health Administration Permissible Exposure Limit) were used as the lowest dose tested. CS₂ was tested at 20 or 40 ppm. The estimated equivalent oral doses were 5 and 10 mg/kg for rats and 11 and 22 mg/kg for rabbits. Both species were exposed for 6-7 hours/day, rats on gestation days 1-19 and rabbits days 1-24. The target number of litters/group was 30 for rats and 20 for rabbits. Cesarean sections were performed on gestation day 21 for rats and 30 for rabbits. The available information does not indicate the number of animals per group. However, the authors report that there was no evidence of teratogenic effect for CS₂ in either species tested.

Price et al., in 1984, administered CS₂ to CD rats on gestation days 6-15 by gavage at 0, 100, 200, 400, or 600 mg/kg/day where significant reductions were observed in fetal weight at 100 mg/kg/day. No significant differences were observed in the incidence of malformations or resorptions at any dose level. Significant reductions in maternal body weight were observed at all dose levels.

Also in 1984, Price et al., evaluated CS₂ for developmental toxicity in New Zealand White rabbits when administered by gavage days 6-19 of gestation at 0, 25, 75, or 150 mg/kg/day in corn oil. Significant maternal toxicity and increased maternal liver weight were observed at 75 and 150 mg/kg/day. The percent resorptions/litter was significantly increased at all dose levels (12.30, 32.47, 41.60, and 61.16% in the 0, 25, 75, or 150 mg/kg/day groups, respectively). The increase in percent resorptions/litter was observed at the

lowest dose tested, 25 mg/kg/day, in the absence of maternal toxicity. The Agency has established the oral RfD for CS₂ based on the combined results of the Hardin et al., 1981 and the Price et al., 1984 studies. The available database indicates that the rabbit is more sensitive to the developmental effects of CS₂ than the rat. Because adverse effects were observed in the Price et al., 1984 rabbit study at 25 mg/kg (25 mg/kg/day = LOEL), the highest NOEL (11 mg/kg/day) is the estimated low dose from the Hardin et al., 1981 study. The Agency has established the oral RfD for CS₂ based on the findings in the inhalation and oral rabbit developmental toxicity studies (NOEL 20 ppm or 11 mg/kg/day oral equivalent) with a 100 fold uncertainty factor (USEPA/OHEA, 1986).

CS₂ is a known neurotoxin in humans, and there are no available data for a "no-effect" level of exposure. There are no chronic toxicity studies available for carbon disulfide, but a 90-day inhalation study in rats is available (MRID # 416288-04, Toxigenics Report # 420-0711B, DER dated 12/16/91). In that study, they evaluated CS₂ at the following dose levels: 50, 300 or 800 ppm. The lowest dose tested, 50 ppm (approx. 27 mg/kg/day, in humans), was NOT shown to be a no-effect dose level. Therefore 50 ppm is an effect level [no NOEL for effect on brain weight]. Effects observed in that study include ataxia, foot drag, axonal swelling of ventral and lateral funiculi of the spinal cord, segmented degeneration in the peripheral nerves. None of the other inhalation data available on CS₂, meet the Agency's guideline requirements (L. Taylor/HED, 8/9/93).

III. EXPOSURE ASSESSMENT

A. *Physical and Chemical Properties Affecting Routes of Exposure*

Although metam sodium probably has no measurable vapor pressure since it is a salt, a solution of metam sodium has a vapor pressure of 21 mm Hg at 25°C. Metam sodium is very stable at a pH greater than 8.8. The commercial metam sodium formulation consists of 32.7% of the active ingredient in water, which is stable at a buffered pH of about 10 (Amvac, 1991; Herbicide Handbook, 1983). Metam sodium is not stable at a pH below 7 and readily hydrolyses.

EFGWB has reviewed a metam sodium aqueous photolysis study (MRID 41517701) (E. Regelman/EFED, 11/5/91). The review states that the registrant reports that under experimental conditions, the metam sodium half life was 11.9 minutes in an aqueous buffered solution irradiated with a filtered xenon arc lamp at 25°C with a pH of 7 (equivalent to 27.8 minutes of natural California sunlight). Under normal agricultural use conditions, metam sodium is diluted with water and sprinkled or injected into the soil. Dilution with water causes its pH to decrease, leading to the rapid hydrolysis of metam sodium. This hydrolysis process produces the following major products- MITC, CS₂, and H₂S, and the subsequent minor products - elemental sulfur and 1,3-dimethylthiourea. Upon hydrolysis, one mole of metam sodium would yield approximately two moles of MITC which causes the pesticidal activity. Carbon disulfide can be produced from metam sodium by an H⁺-catalyzed reaction, but this pathway is minimal at neutral pH (OEEHA/CAL-EPA, 9/21/92).

1. Inhalation Exposure to Metam Sodium

Inhalation exposure to metam sodium is assumed to be negligible because metam sodium readily degrades to MITC, CS₂ and other products. As the handler loads metam sodium into the applicator tank or sprinkler system, water is simultaneously added. As indicated above, the physical and chemical properties of metam sodium cause it to have a short half life as it comes in contact with air and water. The potential exposure under the

current use conditions to both handlers and residents/bystanders would be to the degradation products and not metam sodium.

2. Dermal Exposure to Metam Sodium

Exposure to metam sodium may be via the dermal route, however OREB assumes this route of exposure to be minimal to handlers, and none to residents/bystanders. Since the surface of human skin has an acidic environment with pH in the range of 4.5-6 (J. Olishifski, 1971), and the pH of sweat (E. Emmett, 1986) is about 5, metam sodium is expected to undergo transformation to its degradates after it comes into contact with human skin. CAL-EPA provided OREB with their dermal exposure assessment on metam sodium (J. Donahue/WHSB, 5/16/94). OREB reviewed this assessment and is in agreement with its methodology and conclusions.

To provide potential dermal exposure estimates, they assumed that the dermal absorption to be 2.5%. This rate was determined from an absorption study of ¹⁴C-metam-sodium in rats conducted at the following doses: 8.6, 86.2, and 862 ug/cm² administered to the dorso-lumbar skin sites. The exposure times were 1, 2, 10, 24, and 10 which corresponded to the sacrifice time 1, 2, 10, 24, and 72 hours, respectively. It is important to note that no accurate determination could be made whether the 2.5% absorption was to metam sodium only, and/or including the degradation products. Since no data are available for metam sodium dermal exposure, CAL-EPA used sodium tetrathiocarbonate, as a surrogate. Method of applications were furrow, above ground drip and mini-sprinklers. The average application rate for these sites was 136 lbs ai/acre, and injection of this product into an irrigation system was done through a closed system. The Worker Protection Standard (WPS) PPE requirements for this chemical are identical to that of metam sodium. The application time ranged from 5.75 to 11.33 hours averaging 8.31 hours per day. As sodium tetrathiocarbonate like metam sodium is unstable in the environment, dermal monitoring of active ingredient residue samples was not possible. Therefore, a surrogate chemical, cesium ion in the form of cesium chloride, was added to the product before application at a rate of 0.0975% by weight. Estimation of dermal exposure per day was based on the amount of sodium tetrathiocarbonate that was proportional to the amount of detected cesium ion. Using the above data, CAL-EPA then adjusted the dermal exposure estimates for metam sodium based on the maximum label rate of 318 lbs ai/acre. CAL-EPA utilized the following conservative assumptions:

- a) At least 50% of metam sodium will transform to its metabolites in an 8-hr workday;
- b) 2.5% dermal absorption;
- c) Exposure duration to be 8-hr day and;
- d) Body weight of adult males to be 75.9 kg.

Their absorbed daily dose was estimated to be 0.87 ug/kg/day for either the mixer/loader or applicator. They concluded that the dermal exposure to metam sodium is very low, and that exposure to handlers is primarily by the inhalation route of the degradation products MITC and CS₂.

3. Inhalation Exposure to MITC and CS₂

As indicated above, metam sodium rapidly hydrolyses under acidic conditions. In addition, the PPE and dry disconnect (closed system) requirements for both the loading and application process would decrease the potential of dermal contact to metam sodium. Consequently, the exposure to handlers is primarily via inhalation of the degradation products

MITC and CS₂. Therefore, OREB requested that the registrants monitor inhalation exposure to both MITC and CS₂, and the requirement of dermal monitoring of the parent compound, metam sodium, was waived (A. Mehta/HED, 8/28/91).

B. Current WPS and Other Labelling Requirements

Handlers performing direct-contact tasks are required to wear the following personal protective equipment (PPE) (EPA/OPP, 11/93):

Coveralls over long sleeved shirt and long pants; waterproof gloves; chemical resistant footwear plus socks; chemical resistant headgear for overhead exposure; chemical resistant suit when cleaning equipment, or when mixing, loading, or transferring without dry disconnect fittings; face sealing goggles, unless full-face respirator is worn; and, a respirator with either an organic -vapor-removing cartridge/canister with a prefilter approved for pesticides.

Handlers in Enclosed Cabs, must wear coveralls, shoes and socks, plus face-sealing goggles, unless a full-face respirator is worn, and a respirator with either an organic -vapor-removing cartridge or canister with a prefilter approved for pesticides, if a pungent, rotten-egg odor of this product can be detected inside the enclosed cab.

Handlers in treated areas while entry is restricted (72 hr REI) must wear: coveralls over long-sleeved shirt and long pants, waterproof gloves; chemical resistant footwear and socks; plus face-sealing goggles, unless a full-face respirator is worn, and a respirator with either an organic -vapor-removing cartridge or canister with a prefilter approved for pesticides, if a pungent, rotten-egg odor of this product can be detected.

C. Worker Exposure Estimates to MITC and CS₂

The Occupational and Residential Exposure Branch (OREB) completed a worker and exposure assessment for metam sodium in May 1994 (A. Mehta/HED, 5/5/94). The exposure assessment was based on two Mixer/Loader/Applicator (MRID #'s 429684-02 and 429684-01) studies.

1. Exposure Data Used

One study was conducted in Yuma County, Arizona which measured inhalation exposure to MITC and CS₂ during the following application methods: shank injection and solid set sprinkler, a type of chemigation method. A total of 20 mixer/loader and 20 applicator replicates were collected for the above two application methods/chemical.

The second study was conducted in Grant County, Washington where exposures to MITC and CS₂ were monitored during the following two application methods: rotary tiller injection and center pivot sprinkler, a second type of chemigation method. A total of 15 Mixer/Loader (10 Rotary tiller, 5 center pivot), and 15 applicator (10 rotary tiller and 5 center pivot) replicates were collected. Both studies were conducted using the maximum label rate of 318 lbs ai/treated acre (100 gallons per acre).

Inhalation exposure to MITC and CS₂ was measured utilizing charcoal vapor-collection tubes (400/200 mg, SKC Model Number 226-09). A drying tube to trap moisture was placed in front of each charcoal tube. The drying tubes used in front of the CS₂ sampling

tubes contained sodium sulfate; silica gel drying tubes were used for the MITC samples. Each worker wore two personal air-sampling pumps (MSA Model S,G or Flow-Lite H or SKC Model 224-43XR) on his belt, one to trap CS₂ and the other to trap MITC. Tygon tubing attached the pump to the charcoal vapor-collection tube, which, in turn, was attached to the drying tube and clipped to the worker's collar or lapel near his breathing zone. Prior to the start of each replicate, each air-sampling pump connected to the sampling media was calibrated using a Kurz Mass Flow Meter to an airflow rate of 1.0 liters per min for samples analyzed for MITC and to 0.5 Lpm for samples analyzed for CS₂. The pumps were placed on the worker and turned on at the start of each sampling replicate.

2. Use Information

BEAD provided the following use and usage information:

Metam sodium is primarily used on the following major (> 1000K lbs ai usage per crop) sites: potatoes; row crops and vegetables (including carrots, eggplant, leafy vegetables); peanuts; and cole crops (G. Tomimatsu/BEAD, 1/21/93). It is applied with either tractor-driven, shank injection machinery or through chemigation equipment. The chemical is delivered by the company to the grower (who may use storage containers ranging from 700 to 4000 gallons), or to bulk storage tanks (up to 7700 gallon capacity) near fields. When metam sodium is applied, tarping is not used. Instead, the soil is "water-sealed." The overall dosage range for all crops and methods of application is 127 to 318 lbs ai/treated acre. The remaining use/usage information is categorized by site.

For crops treated via either the shank or rotary tiller method (e.g. peanuts), the chemical is pumped with an electric pump (and metered) into the applicator tank. Overflow is checked with orifice disks and check valves. Applications are made with a 4-row or 8-row injector (w/ an average 120 gallon tank) on a field with 36" row spacing. One or two workers can treat about 25-30 acres of peanuts in a 6 - 8 hr workday. After 2 or 3 weeks, growers plant peanuts on top of the bed.

For row and vegetable crops, the 3000-4000 gallon tanks are commonly used for loading purposes. The tanks are placed near the wells; a booster pump is then placed near the water source. The distributor will do the calibration and help the grower with the loading. The grower can treat 10-15 acres in an 8-10 hr day, using a stationary (solid set) sprinkler. Note that the range of "hrs/day" depends upon the amount of water that needs to be applied. For the shanking applications, a grower will pre-irrigate the field and the distributor/custom applicator will deliver and inject the chemical 12 to 14" deep into the soil. A bed shaper follows to shape and seal the soil. Carrots, for example, are then planted 14 days to 1 month after application.

For crops treated via the center pivot chemigation method, metam sodium is delivered by the custom applicator to a bulk storage tank (5500 gallon capacity) that is located on site. The entire mixing/loading and application is via a closed system; one worker is necessary, but usually two are available to monitor the chemigation.

3. Assumptions

The route of exposure for both MITC and CS₂ is inhalation, and OREB assumes that absorption is 100%. From the use information provided by BEAD, OREB assumes that there are two people involved in the mixing/loading and application. Since the toxicity endpoints for both MITC and CS₂ are developmental, OREB has provided exposure estimates for females whose average body weight is assumed to be 60 kg, and the ventilation rate is 14

assumed to be 0.96 m³/hr for moderate work. The number of hours exposed for the mixer/loader is 0.5 hr/day, and for the applicator is 8 hrs/day. Although there are insufficient data to determine the distribution, environmental data are often lognormal; hence, OREB assumes that personal air monitoring concentrations do follow a lognormal distribution. Therefore, the geometric mean is used as the measure of central tendency for the exposure calculations.

4. Exposure Estimates and Sample Calculation

TABLE 1: MITC Estimates of Handler Exposure for Each Application Method

Application Type	No. of Reps.	MIXER/LOADER		APPLICATOR		
		Inhal. Conc. Geometric Mean (ug/m ³)	Exposure (mg/kg/day) MITC (females)	No. of Reps.	Inhal. Conc. Geometric Mean (ug/m ³)	Exposure (mg/kg/day) MITC (females)
SHANK INJECTION	10	326.42	2.61 x 10 ⁻³	8	1034.20	1.32 x 10 ⁻¹
ROTARY TILLER INJECTION	10	452.56	3.62 x 10 ⁻³	5	600.92	7.69 x 10 ⁻²
SOLID SET SPRINKLER (chemigation)	10	440.19	3.52 x 10 ⁻³	10	892.75	1.14 x 10 ⁻¹
CENTER PIVOT SPRINKLER (chemigation)	5	203.60	1.63 x 10 ⁻³	5	89.82	1.15 x 10 ⁻²

Replicates that were run with Charcoal Filtered Cabs were not included.

Sample Calculation:

(Shank Injection): Mixer/loader: MITC (female only) Exposure (mg/kg/day) =

$$= \frac{(\text{Inhal. Conc. ug/M}^3) * (\text{Ventil. Rate}) * (1 \text{ mg}/1000 \text{ ug}) * (\text{Exp.dur. hrs/day})}{60 \text{ kg}}$$

$$= \frac{(326.42 \text{ ug/m}^3) * (0.96 \text{ m}^3/\text{hr}) * (1 \text{ mg}/1000 \text{ ug}) * (0.5 \text{ hrs/day})}{60 \text{ kg}}$$

$$= 2.61 \times 10^{-3} \text{ mg/kg/day}$$

(Shank Injection): Applieator: Exposure (mg/kg/day) =

$$= \frac{(\text{Inhal. Conc. ug/M}^3) * (\text{Ventil. Rate}) * (1 \text{ mg}/1000 \text{ ug}) * (\text{Exp.dur. hrs/day})}{60 \text{ kg}}$$

$$= \frac{(1034.20 \text{ ug/m}^3) * (0.96 \text{ m}^3/\text{hr}) * (1 \text{ mg}/1000 \text{ ug}) * (8.0 \text{ hrs/day})}{60 \text{ kg}}$$

$$= 1.32 \times 10^{-1} \text{ mg/kg/day}$$

TABLE 2: CS₂ Estimates of Handler Exposure for Each Application Method

Application Type	MIXER/LOADER			APPLICATOR		
	No. of Reps.	Inhal. Conc. Geometric Mean (ug/m ³)	Exposure (mg/kg/day) CS ₂	No. of Reps.	Inhal. Conc. Geometric Mean (ug/m ³)	Exposure (mg/kg/day)CS ₂
<i>SHANK INJECTION</i>	10	519.37	4.15 x 10 ⁻³	8*	50.23	6.42 x 10 ⁻³
<i>ROTARY TILLER INJECTION</i>	10	594.05	4.75 x 10 ⁻³	5*	68.74	8.79 x 10 ⁻³
<i>SOLID SET SPRINKLER (chemigation)</i>	10	43.94	3.51 x 10 ⁻⁴	10	10.69	1.36 x 10 ⁻³
<i>CENTER PIVOT SPRINKLER (chemigation)</i>	5	417.62	3.34 x 10 ⁻³	5	17.90	2.29 x 10 ⁻³

Replicates that were run with Charcoal Filtered Cabs were not included.

Sample Calculation:

(Shank Injection): Mixer/loader: CS₂ (female only) Exposure (mg/kg/day) =

$$= \frac{(\text{Inhal. Conc. ug/M}^3) * (\text{Ventil. Rate}) * (1 \text{ mg}/1000 \text{ ug}) * (\text{Exp.dur. hrs/day})}{60 \text{ kg}}$$

$$= \frac{(519.37 \text{ ug/m}^3) * (0.96 \text{ m}^3/\text{hr}) * (1 \text{ mg}/1000 \text{ ug}) * (0.5 \text{ hrs/day})}{60 \text{ kg}}$$

$$= 4.15 \times 10^{-3} \text{ mg/kg/day}$$

(Shank Injection): Applicator: Exposure (mg/kg/day) =

$$= \frac{(\text{Inhal. Conc. ug/M}^3) * (\text{Ventil. Rate}) * (1 \text{ mg}/1000 \text{ ug}) * (\text{Exp.dur. hrs/day})}{60 \text{ kg}}$$

$$= \frac{(50.23 \text{ ug/m}^3) * (0.96 \text{ m}^3/\text{hr}) * (1 \text{ mg}/1000 \text{ ug}) * (8.0 \text{ hrs/day})}{60 \text{ kg}}$$

$$= 6.43 \times 10^{-3} \text{ mg/kg/day}$$

B. Residential Exposure to MITC Only

1. Exposure Data Used

A Downwind/Bystander Exposure study was submitted by the MSTF in 1993. OREB reviewed this study (MRID # 426599-01) and found it to be acceptable (A. Mehta/HED, 5/5/94). The study was conducted to provide dissipation and volatility data for the principle degradation product, MITC, during and after application. Since the worker exposure studies illustrated that the collected CS₂ concentrations were nominal, the MSTF requested that for the residential/bystander study only MITC be sampled. OREB agreed to this protocol change.

This study was also performed to assess exposure to bystanders/residents near fields treated with metam sodium. The solid set sprinkler application method was chosen by the MSTF to assess residential risk because it represents a worst case scenario as far as spray drift is concerned.

The study was conducted in Madera County near Firebaugh, California on May 2 through May 4, 1992, using solid set sprinklers. Busan 1020 (water miscible concentrate, minimum 32.7% active ingredient metam sodium, manufactured by Buckman Laboratories, Inc.) was applied to bare ground at the maximum label rate of 318 lbs ai/treated acre (100 gallons per acre) to a field of 6.69 acres in a four hour period.

Downwind sampling stations were established perpendicular to the prevailing northwest wind direction at 5, 25, 125, and 500 meters (16.40, 82.0, 410.10, and 1640.42 feet) from the downwind edge of the application swath. Each station consisted of three T-posts and a high volume air sampling pump (SKC catalog number 228-501) connected by flexible tubing to two charcoal vapor collection tubes (400/200 mg, SKC catalog number 226-09). The charcoal tube was preceded by a silica gel drying tube (200/100 mg, SKC catalog number 226-10-06) and a plastic cassette containing a glass fiber filter and support pad; these were used to trap moisture and to screen out dust particles, respectively. The charcoal and silica gel tubes were placed inside a hollow plastic pipe to protect them from physical damage and hung from the T-posts at a height of 1.5 meters. Monitoring commenced at start of application and continued for 48 hrs after application (52 hours total). Charcoal tubes were changed every four hours.

2. Use Information Provided by BEAD

The solid set sprinkler chemigation method is primarily used for row crops and vegetables, including carrots, eggplant, and leafy vegetables. A grower can treat 10 to 15 acres in an 8-10 hrs per workday, using a stationary sprinkler. The range of hrs-day depends upon the amount of water that needs to be applied.

3. Assumptions

OREB's assumptions were the following:

Ventilation Rate (females): 0.81 m³/hr (20 m³/day) (adult, average; USEPA/ORD, 3/90)

Exposure Duration: 24 hrs or 1 day

Concentration: ug/m³, indoor = outdoor

Inhalation Absorption: 100%

Female body weight: 60 kg

4. Exposure Estimates and Sample Calculations

The following table provides MITC exposure estimates to residents living downwind from the field.

Sample Calculation: Avg. Daily Exposures (500 meters)

$$\begin{aligned}
 & \text{(Sample Interval: 0-24): Bystander/Resident Exposure (mg/kg/day) =} \\
 & \frac{(\text{inhal. conc. ug/m}^3) * (\text{Ventil. rate}) * (1 \text{ mg}/1000 \text{ ug}) * (\text{Exp.dur. hrs/day})}{60 \text{ kg}} \\
 & = \frac{(68.32 \text{ ug/m}^3) * (0.81 \text{ m}^3/\text{hr}) * (1 \text{ mg}/1000 \text{ ug}) * (24 \text{ hrs/day})}{60 \text{ kg}} \\
 & = 2.21 \times 10^{-2} \text{ mg/kg/day}
 \end{aligned}$$

TABLE 3: Bystander/Residential Exposure Estimates to MITC using Downwind Sampling Data

Sample Interval (hrs)	Soil Type	Distance (meters)	Inhal. Conc. Range (ug/m ³)	Inhal. Conc. Arith. Mean (ug/m ³)	Exposure (mg/kg/day) (females)
0-24	Loamy Sand	5.0	50.75 - 1254.50	564.88	183 x 10 ⁻³
0-24	Loamy sand	25.0	38.25 - 1042.50	511.20	165.6 x 10 ⁻³
0-24	Loamy sand	125.0	60.40 - 818.00	354.32	114.8 x 10 ⁻³
0-24	Loamy sand	500.0	8.77 - 163.00	68.32	22.14 x 10 ⁻³

V. RISK CHARACTERIZATION

A. Margin of Exposure (MOE) Estimates

On comparison of the developmental toxicology database of metam sodium with MITC it is apparent that MITC is more toxic. In addition, the spectrum of adverse effects resulting from MITC exposure differs from that observed from metam sodium exposure. Due to the chemical nature of metam sodium, in that it readily hydrolyses to MITC and CS₂, OREB anticipates that actual exposure would be to MITC and CS₂ rather than metam sodium. Therefore, the MOE's were derived based on comparison of exposure estimates against the (developmental toxicity) NOEL of 3 mg/kg/day for short term exposures to MITC. For short term exposure to CS₂, the NOEL of 11 mg/kg/day was used which is based on a rabbit inhalation teratology study. Tables 4 and 5 contain the exposure estimates plus the calculated MOE's. Risk estimates should be considered conservative as they were calculated assuming the maximal application rate of 318 lbs ai/treated acre.

TABLE 4: MITC Handler MOE's for Each Application Method

	<i>MIXER/LOADER</i>		<i>APPLICATOR</i>	
Application Method	Acute Exposure (mg/kg/day) MITC (females)	MOE (NOEL = 3 mg/kg/day)	Acute Exposure (mg/kg/day) MITC (females)	MOE (NOEL = 3 mg/kg/day)
<i>Shank Injection</i>	2.61×10^{-3}	1149	1.32×10^{-1}	23
<i>Rotary Tiller Injection</i>	3.62×10^{-3}	829	7.69×10^{-2}	39
<i>Solid Set Sprinkler (chemigation)</i>	3.52×10^{-3}	852	1.14×10^{-1}	26
<i>Center Pivot Sprinkler (chemigation)</i>	1.63×10^{-3}	1840	1.15×10^{-2}	261

Sample Calculation: Acute MOE's

Shank Injection:(Applicator: Acute/ Daily Exposure):

$$\text{MOE} = \frac{\text{NOEL mg/kg/day}}{\text{Expos.mg/kg/day}} = \frac{3 \text{ mg/kg/day}}{1.32 \times 10^{-1}}$$

= 23

TABLE 5: CS₂ Handler MOE's for Each Application Method

	<i>MIXER/LOADER</i>		<i>APPLICATOR</i>	
Application Type	Acute Exposure (mg/kg/day) CS₂ (females)	MOE (NOEL = 11mg/kg/day)	Acute Exposure (mg/kg/day) CS₂ (females)	MOE (NOEL = 11 mg/kg/day)
<i>Shank Injection</i>	4.15×10^{-3}	2651	6.42×10^{-3}	1713
<i>Rotary Tiller Injection</i>	4.75×10^{-3}	2316	8.79×10^{-3}	1251
<i>Solid Set Sprinkler (chemigation)</i>	3.51×10^{-4}	31339	1.36×10^{-3}	8088
<i>Center Pivot Sprinkler (chemigation)</i>	3.34×10^{-3}	3293	2.29×10^{-3}	4803

Sample Calculation: Acute Toxicity

$$\text{MOE} = \frac{\text{NOEL mg/kg/day}}{\text{Expos.mg/kg/day}} = \frac{11 \text{ mg/kg/day}}{6.42 \times 10^{-3}}$$

$$= 1713$$

TABLE 6: MITC Bystander/Residential MOE's Using Samples Collected Downwind

Sample Interval (hrs)	Distance (meters)	Acute Exposure (mg/kg/day) (females)	MOE (NOEL = 3 mg/kg/day)
0-24	5.0	183.0 x 10 ⁻³	18
0-24	25.0	165.6 x 10 ⁻³	18
0-24	125.0	114.8 x 10 ⁻³	28
0-24	500.0	22.14 x 10 ⁻³	135

Sample Calculation: Acute Exposure

(Sample Interval:0-24); 500 meters

$$\text{MOE} = \frac{\text{NOEL mg/kg/day}}{\text{Expos.mg/kg/day}} = \frac{3 \text{ mg/kg/day}}{22.14 \times 10^{-3}}$$

$$= 135$$

V. STRENGTHS AND UNCERTAINTIES OF THE RISK ASSESSMENT

The metam sodium worker and residential/bystander risk assessment contains uncertainties that are the result of data gaps and/or lack of scientific knowledge. Standard assumptions were used to estimate worker and residential/bystander risks including inter-species extrapolation.

The developmental NOEL from the MITC developmental toxicity study in rabbits was deemed tentative by the HED Developmental and Reproductive Peer Review Committee, and should be viewed as an uncertainty. Further information has been requested to upgrade the study, and hence, the NOEL may potentially change.

HED used exposure data collected from the new worker and residential/bystander studies. Both of these studies were conducted using the maximum application rate of 318 lbs ai/treated acre; hence, it is possible that risks would be lower for applications made using a lower rate. The use/usage database for metam sodium is not complete. The residential/bystander MOE's were calculated for only one application method, i.e. the solid set sprinkler chemigation. No data are available for the other three application methods.

VI. CONCLUSION

OREB has provided the exposure and risk estimates for both the worker and residential population. Exposures to the degradation products- MITC and CS₂ for handlers and MITC, alone, for residents/bystanders are primarily via the inhalation route. Inhalation and dermal exposure to the parent compound, metam sodium, is considered to be negligible. The MITC applicator MOE's for three out of the four types application methods are below 100. It is worth noting that in the first worker exposure study, two out of the 10 applicator replicates during shank injection, were taken in a positive pressure charcoal filtered enclosed tractor cab. Exposure estimates using those two replicates were approximately 30% lower; however in the second study, five out of the 10 replicates were measured in an charcoal filtered enclosed cab; and, again two out of the five replicates provided lower exposure estimates. Although there is no Enclosed Cab Tractor Standard that requires manufacturers to meet certain performance criteria, at the present time; the use of this mitigation technique must be encouraged in the agricultural industry as it has the potential of greatly reducing exposure to MITC. The present label according to the WPS guidance on metam sodium, requires handlers to wear respirators if they are not in an enclosed cab; however, compliance regarding this PPE requirement is known to be low.

The MITC MOE's for mixer/loaders were above 100 for all application methods, while the MITC MOE's for the applicator ranged from 23 to 261.

The CS₂ MOE's for both mixer/loader and applicator were calculated to be greater than 100.

The residential/bystander MITC MOE's at the four distances range from 16 to 135. Bystanders exposed to MITC at < 500 meters (approximately, 1640 feet or 0.31 miles) have MOE's less than 100.

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Attachments

cc: A. Mehta/OREB w/ attach. 7509C
L. Dorsey/OREB 7509C
S. Knott/OREB 7509C
P. Crisp 7509C
L. Taylor/Tox II w/ attach. 7509C
L. Engstrom/SRB w/ attach. 7508W ✓
M. Ioannou/Tox II 7509C
A. Medici/OGC w/ attach. 2333R ✓
S. Zavolta/BAB 7503W ✓
K. Whitby/CCB w/ attach. 7509C
S. Robbins/RD 7505C ✓
Chemical file ✓
Correspondence ✓
Circulation ✓
Caswell File ✓